UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Briana Hanlon, Risk Manager

From: Robert Drake Mitchell III, Ph.D., Entomologist

Secondary Review: Virna Stillwaugh, Ph.D., Senior Entomologist

Date: 12/17/2021

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 462986
Decision no.: 576885
Submission no: 1071741
Action code: R340
Product Name: In2Mix®
EPA Reg. No or File Symbol: 91720-1
Formulation Type: Powder
Ingredients statement from the label with PC codes included:

Beauveria bassiana GHA 10%	PC: 128924
Pyriproxyfen 74.03%	PC: 129032

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate): Place at least one In2Care® trap every 4,300 sq. feet (400 sq. meters), or at least 10 traps per acre in areas where *Aedes* mosquitoes breeding can be expected. Do not exceed 15 traps per acre. Each trap contains one 0.5 g (0.018 oz.) packet containing 74.03% pyriproxyfen and 10.0% *Beauveria bassiana*. Use one In2Mix® package per trap every 4 weeks when adult mosquitoes are active.

Use Patterns: For use to control *Aedes* species of mosquitoes that may transmit Zika, Chikungunya, and Dengue Fever. The growth regulator kills *Aedes* spp. larvae that emerge from eggs laid inside the trap prior to transforming into adults. After laying eggs, the adult *Aedes* spp. mosquito is contaminated with the In2Mix® powder. When they fly out of the trap to lay more eggs elsewhere, they disseminate the growth regulator and kill larvae in breeding sites around the trap. The adulticide contained in the In2Mix® powder slowly kills adult *Aedes* spp. mosquitoes. Contaminated mosquitoes will die within a few days following exposure to In2Mix® powder. Traps are suggested to be placed outside on the ground in a level, shaded location near human habitation. Avoid locations with direct sunlight; continuous shade is needed.

I. Action Requested: Review requested for one new MRID (51615606) to add additional efficacy claims for mosquitoes.

II. Background: The registrant submitted an application package to add *Culex* spp. and to extend the duration of

control for a registered pyriproxyfen plus *Beauveria bassiana* mosquito trap (Reg. no. 91720-1) onto the label. MRID 51615606 provides efficacy data against *Aedes* and *Culex* mosquitoes.

III. MRID Summary:

MRID 51615606: Möhlmann, T. Farenhorst, M. Buckner, E. et al. (2021). In2Mix A Compilation of Mosquito Efficacy Studies. Project Number: In2Mix/810. Unpublished study prepared by In2Care BV. 81p.

This MRID is a compilation of 6 studies that tested the efficacy of In2Mix® powder (the packet containing both active ingredients) on *Culex* and *Aedes* mosquitoes in a laboratory, semi-field, and field setting when applied to the In2Care® Mosquito Trap. The methods, results, and conclusions for each of the 6 efficacy studies will each be presented separately in this section.

Study #1: Cage Tests against *Culex* Mosquitoes (Wageningen, The Netherlands)

(1) **GLP:** non-GLP

(2) **Methods:** The objective of this study was to investigate if In2Care® Mosquito Traps are attractive to *Culex* mosquitoes and are successful in killing their larvae. Additionally, the registrant tested if the In2Mix® (containing the active ingredients) on the trap netting could kill adult *Culex quinquefasciatus* mosquitoes.

Mosquito preparation: *Culex quinquefasciatus* strain JHB adults were maintained at 27 (±1)°C in 30×30×30 cm Bugdorm® cages (presumably within an indoor insectary, but that was not clearly stated in the text). The room was kept at a relative humidity (RH) of 65 (±5)% under a 12h:12 h L:D (Light:Dark cycle). Mosquitoes had *ad libitum* access to 6% glucose until females were blood-fed (direct arm feeding on humans) at 3-5 days post pupal emergence. Blood-fed females were transferred via aspirator to new cages (50 female *Cx. quinquefasciatus* per cage), given access to 6% glucose, and held for 3 days before testing to allow them to become gravid. *Cx. quinquefasciatus* larvae were reared in tap water and fed Tetramin® fish food daily (amount of food not reported; amount could have impact on survivability). It is unclear if larvae were reared in the same room/facility as the adults under the same environmental conditions. Also, there was no indication if the tap water was treated in any way (for example, dechlorinated) or changed regularly to facilitate larval survival.

Experimental set up: Mosquito release and recapture studies were performed indoors within two large (2.40 m x 3.20 m x 2.20 m) free-flying cages held in test rooms at 26 (±3)°C and a RH of 67 (±7)% during all experiments. In each cage, one In2Care® Mosquito Trap was placed on the floor in the middle and surrounded by 4 clean ovipots, each spaced roughly 1 m from the center trap. The ovipots were clear glass bowls filled with 500 mL tap water and 150 mg alfalfa placed within black plastic flowerpots as a larval food source. They served as alternative breeding sites. A diagram of the test arena showing placement of the trap and ovipots would have been useful to help visualize their orientation within the cages, but it was not provided. The In2Care® Mosquito Trap was described as a 5-Liter polypropylene container (holding 4.5 Liters of water) while the ovipots held only 500 mL in a glass bowl placed within a black flowerpot measuring 16 cm in diameter and a 15 cm depth. The minimum labeled rate of 1 trap per 4300 ft^2 (400 m^2) was not tested.

Attraction test: In a single cage the In2Care® Mosquito Trap (middle) and 4 clean ovipots (surrounding) were situated as described above. To test the attractiveness of the trap to egg-laying adult females it was filled with 4.5 L of water, 2 yeast tablets, and a floating device ("floater") coated with fluorescent powder as shown in Fig. 1. The floater is the part of the trapping device that is used to deliver the active ingredients via a treated gauze strip (but not chemically treated for this test). 100 gravid *Cx. quinquefasciatus* adult females were released into the cage and allowed to lay eggs for 2 days, after which the number of recaptured and dead mosquitoes was recorded. Live recaptured females were then frozen for 2-4 h and imaged under a UV LED-light microscope to visualize any fluorescent powder that was attached to their body, indicating that they had visited the In2Care® Mosquito Trap in the middle of the cage. This test was replicated 4 times (4 powder-treated trap runs in one cage and 4 untreated trap runs in another cage).

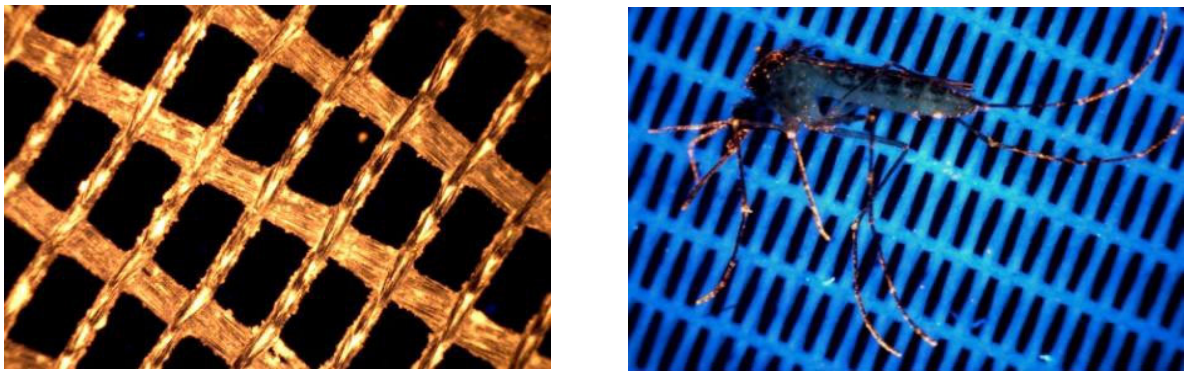

Figure 1. (left) Orange fluorescent powder applied to electrostatically charged gauze from mosquito trap and (right) *Cx. quinquefasciatus* female with fluorescent powder on legs viewed under UV LED-light microscope.

Testing mosquito breeding and adulticidal impacts of the In2Mix: To determine the baseline survival rates of the *Culex* larvae and mosquitoes, Control experiments were performed, each using 4 clean ovipots and 1 clean In2Care® Trap without bioactives in the cage set-up. The Trap was filled with 4.5 Liters of water in which 2 yeast tablets were added, and the floater carried a clean strip of the electrostatic coated netting.

Test replicates were performed by using 4 clean ovipots and 1 In2Care® Mosquito Trap in the cage set-up. To activate the Traps, In2Mix® sachets from batch I2CT.1.US.1002 (EPA Reg. No. 91720-1, production date September 2017) were used containing 74.03% pyriproxyfen and 10% *Beauveria bassiana* strain GHA as active ingredients, as stated on the EPA-registered label. In2Care® Traps were treated with In2Mix® following the Directions For Use on the label. Each Trap was filled with 4.5 Liters of clean tap water, the In2Mix®-treated netting strip was taken out of the refill sachet and attached to the floater, and the floater was gently placed on the water surface. The remaining In2Mix® powder and the 2 yeast tablets from the refill sachet were added to the Trap water.

To test adult mortality, 100 gravid *Cx. quinquefasciatus* adult females were released into a single cage (same configuration as above) and allowed to fly and lay eggs for 2 days, after which all mosquitoes were recaptured with manual aspirators and placed in holding cages with glucose as a food source. The number of recaptured and dead mosquitoes was recorded. The retrieved groups of mosquitoes were monitored for survival daily to assess the adulticidal impact of the *B. bassiana* in the ln2Mix® treated trap versus the clean control trap. In addition, the number of egg rafts in each trap and ovipot were recorded upon retrieval to assess breeding site preference. The number of egg rafts was used as a direct indicator for the number of visiting mosquitoes, assuming 1 egg raft correlates to a single female's eggs.

Larval mortality/adult emergence test: Each In2Care® Mosquito Trap was removed at the completion of the adult experiments and 20 L_3-stage *Cx. quinquefasciatus* larvae were introduced (i.e., 20 larvae per container x 4 baited In2Care® Mosquito Traps = 80 test larvae: 20 larvae per container x 4 unbaited In2Care® Mosquito Traps = 80 control larvae). The traps were covered with mesh and observed for a maximum of 14 days over which time dead larvae, pupae, and percent adult emergence was recorded. Emerged adults were collected and frozen so that they could be counted, and percent adult emergence was used as a proxy for larvicidal impact.

Statistical analyses: Statistical analyses were done using SPSS 23.0 software. Normality of the data was investigated using the Shapiro-Wilk Test. Comparisons of egg raft collections between Control and Test replicates were done using independent sample T-tests for normally distributed data and a Mann-Whitney U test for data that were not normally distributed. Analyses of larvicidal impact were done using a one-way ANOVA test followed by a Tukey post-hoc test. Differences in mosquito survival between the retrieved Control groups and Test groups were analyzed using Cox Regression. Survival curves were made by pooling the mortality data for both groups and Hazard Ratio (HR) values, indicating the average daily risk of dying between the two groups, were computed to measure significant differences in overall mortality rates. To justify the proportional hazard assumption, plots of survivor functions were used to check Hazard Ratio proportionality.

(3) **Results:**

Attractiveness of the ln2Care® Mosquito Trap**:** After 2 days, 90.8% of the released *Cx. quinquefasciatus* adult females were recovered and an average of 95% of them visited the fluorescent powder-treated In2Care® Mosquito Trap and rested on the floater in the attraction test at some point during the 2-day egg-laying period.

In the Control replicates (where a clean In2Care® Trap was used), on average 90.3% of the released *Culex* mosquitoes were retrieved. Egg raft counts showed that on average 83.8% of the gravid mosquitoes in the control groups had laid an egg raft. The Test replicates with an In2Mix®-baited In2Care® Trap showed similar recapture rates; 89.5% (P>0.05) and equal mosquito breeding success; 81.3% (P>0.05).

In the control experiment (unbaited trap) there was an average of 10 egg rafts laid per ovipot and 46 egg rafts laid in the clean In2Care® Mosquito Trap. In the experimental (baited trap) runs there were 10 egg rafts laid per ovipot and 43 egg rafts in the treated In2Care® Mosquito Trap. There was a significant difference in both experiments (P>0.05). If the ovipots would have been equally attractive to the In2Care® Trap, an equal egg distribution (20% in each site) would have been observed. The fact that on average 54% of all eggs were laid inside the In2Care® Trap in the Control experiment and 52% inside the In2Care® Trap in the Test replicates, indicates that the Traps are more attractive as breeding site. The difference in the egg raft proportions between the clean Control In2Care® Trap and biocide-treated In2Care® Trap was not significant (P>0.05), which demonstrates that the presence of the In2Mix® biocide powders does not negatively affect the attraction to mosquitoes.

Larvicidal impacts of the Ln2Mix®: Results showed that in the clean Control Traps, on average 75% of the added larvae fully developed and emerged as adult *Culex* mosquitoes. In contrast, from the In2Mix®-baited Traps 0% adult emergence was observed (Fig. 2). All Culex larvae in this Test group were killed in the late L4 stage or pupal stage, and dead pupae showed a distinct black color and de-curling of the tail which is distinct for pyriproxyfen-induced molting inhibition. This means there was 100% adult emergence inhibition in the Test group with In2Care® Mosquito Traps.

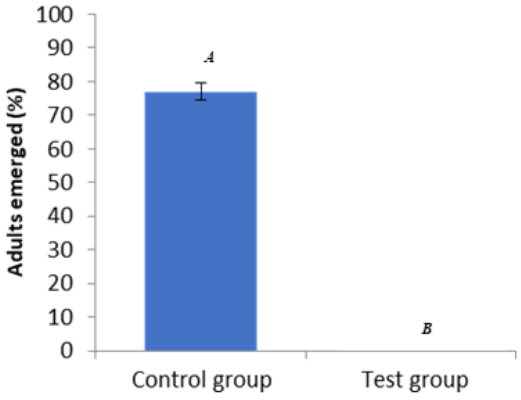

Figure 2. *Culex* adult mosquito emergence.

Adult mosquito survivorship was significantly reduced when an In2Care® Trap with In2Mix® (containing *Beauveria bassiana* spores) was deployed in the cage (Fig. 3). Cox regression analyses showed significant differences in survival curves of *Culex* cohorts between the control and treatment groups. The presence of only 1 In2Mix®-baited In2Care® Trap induced significantly lower survivorship rates in *Culex quinquefasciatus* compared to the Control experiment with a clean Trap (HR=28.22; P<0.001).). The survival curves show a sigmoid decline that is typical of *Beauveria*-induced lethality, killing the majority of the exposed mosquitoes within 8 days.

An average of 90.3% and 89.5% of the 100 gravid females were recaptured alive in the control and experimental replicates after 2 days, respectively. As shown in Fig. 2, an average of 80% of the retrieved

females died within 8 days of exposure to the treated trap versus 40% control mortality at that same time point. The mosquitoes in the controls only approached 80% mortality after 18 days.

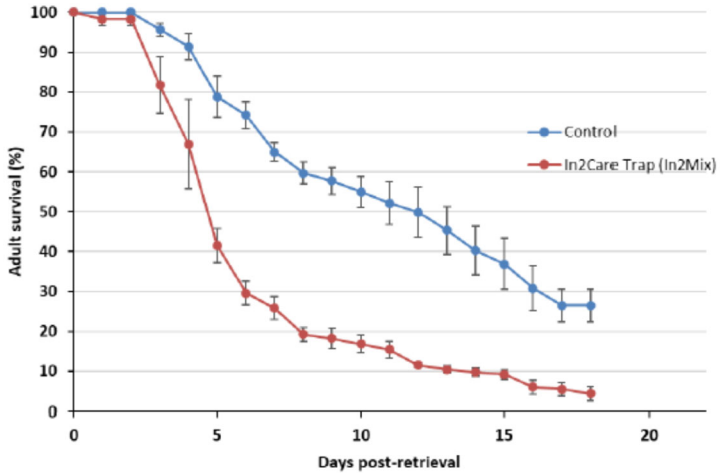

Figure 3. Female adult *Cx. quinquefasciatus* percent survival.

(4) **Conclusions: Supplemental**. The minimum labeled rate of 1 trap per 4300 ft^2 (400 m^2) was not tested. This study demonstrated that the In2Care® Mosquito Trap (baited with In2Mix®) prevents *Culex* adult emergence for up to 14 days, and that *Culex* mosquitoes are attracted to the traps (baited and unbaited). Additional field data testing the minimum labeled rate should be submitted to support efficacy claims. Kills/Controls claims for adult *Culex* are not supported. Kill claims for adult *Culex* mosquitoes are not supported as treated traps mortality was 80% (never reached 90%) and control mortality at the same time point was 40%. Therefore, claims of reducing adult survivability and/or accelerating adult mortality are also unacceptable.

Kills/controls claims for larvae are not supported. No data was supplied that specifically demonstrated larval or pupal mortality and the only endpoint that was reported was successful or unsuccessful adult emergence. In addition, the fluorescent powder experiment simply showed that the mosquitoes visited the trap sometime during the 2-day exposure period, but there was no indication from that experiment that the trap was preferred for egg laying over the alternate landing sites as they could have visited one site but subsequently laid their eggs at another site. No egg counts were reported for that experiment as well. However, the experiment where adult egg laying behavior was recorded did support attraction claims since egg rafts were counted at the trap and the surrounding alternate breeding sites. That study showed that roughly 4X as many eggs were laid in the trap as were laid in the surrounding ovipots.

The high control mortality in the adult study could be attributed to the type/quality of the water that was used for the studies. Some mosquito species thrive in clear water while others survive better in stagnant, nutrient-rich water. Tap water may not be ideal for this species and other water types should be investigated, like well water that is typically rich in minerals. It was also never specified whether the tap water was treated (for example, dechlorinated), which could also have an impact on *Culex* survival. There was also the possibility of cross contamination confounding the results since one of the active ingredients is a microbial insecticide and not easy to handle.

Population reduction claims are not supported. To obtain population reduction claims an experimental design including (a) assessment of "residual activity" of the product and (b) 'pre' and 'post' treatment mosquito counts at the test site are the currently accepted standard (e.g., sweeps or CDC traps). In addition, it is preferable that the counting method does not rely on traditional landing counts in light of the potential risk for mosquito-borne disease transmission.

Study #2: Semi-Field Test against *Culex* Mosquitoes (Vero Beach, Florida)

(1) **GLP:** non-GLP

(2) **Methods:** The objectives of the study were to assess attraction and the larvicidal, autodissemination, and adulticidal impacts of In2Mix®-baited In2Care® Mosquito Traps against locally sourced *Culex quinquefasciatus* mosquitoes under ambient climate conditions in Florida, USA.

Mosquito preparation: *Culex quinquefasciatus* adults were maintained at 27 (±2)°C in 30×30×30 cm Bugdorm® cages (it was unclear if it was in an indoor insectary). The room was kept at a relative humidity (RH) of 75 (±10)% under a "natural" light cycle (specific light cycle timing was not specified). The mosquitoes had *ad libitum* access to a 6% glucose solution until the females were blood-fed (human blood through a membrane) at 3-6 days post pupal emergence. Blood-fed females were transferred via aspirator to new cages (50 females per cage), given access to 6% glucose, and held for 3 days before testing to allow them to become gravid. *Cx. quinquefasciatus* Larvae were reared in osmosis-filtered tap water and fed fish food and/or yeast daily (amount of food not reported; amount could have impact on survivability). It was unclear to the reviewer if the larvae were reared in the same room/facility as the adults under the same environmental conditions from the provided description. Semi-field trials were conducted with wild-type F1 *Cx. quinquefasciatus* female adults reared from egg rafts collected at various sites around Florida in 2019. Fungus testing was conducted with wild-type F1 *Cx. quinquefasciatus* female adults reared from egg rafts collected at various sites in Miami-Dade County (Florida) in 2020.

Test arena: Mosquito release and recapture studies were performed in two adjoining 8 ft. x 8 ft. mesh screen rooms exposed to ambient outdoor conditions. Each room had a sheet metal roof, a dirt floor, and four total *Philodendron bipinnatifidum* plants (one on each wall) to provide resting sites and testing was conducted on days when daytime temperatures were forecasted to be above 68°F (20°C).

In2Care® Mosquito Traps: Experiments used the black plastic In2Care® Mosquito Traps and In2Mix® sachets from batch I2CT.1.US.1021 (EPA Reg. No. 91720-1, production date April 2019) containing 74.03% pyriproxyfen and 10% *Beauveria bassiana* strain GHA as active ingredients. In2Care® Traps were treated with In2Mix® one day before the onset of the experiment following the Directions For Use (DFU) on the label. Each trap was filled with 4.5 Liters of clean tap water, the In2Mix®-treated netting strip was taken out of the refill sachet and attached to the floater, and the floater was gently placed on the water surface. The remaining In2Mix® powder and 2 yeast tablets from the refill sachet were added to the trap water.

Semi-field control experiments: To determine the baseline survival rates of *Culex* larvae and adult mosquitoes, control experiments were performed with 5 clean ovipots. Ovipots consisted of a clear glass bowl (15.2 cm diameter and 7.6 cm depth) containing 400 ml of tap water and 150 mg alfalfa (as larval food source) placed inside a 15.2 cm diameter and 13.9 cm depth black plastic flowerpot. Per control replicate, 5 ovipots were placed at a 2-meter distance from each other in the semi-field screenhouse.

Semi-field autodissemination experiments: To assess the larvicidal impacts in the In2Care® Mosquito Trap and in surrounding ovitraps (potentially contaminated via autodissemination), 5 test replicates were performed with 4 clean ovipots and 1 In2Care® Mosquito Trap in the screenhouse set-up. In each test, 50 gravid *Culex quinquefasciatus* were released in the center of the screenhouse and allowed to fly and lay eggs for 2 days. Afterwards, all mosquitoes were recaptured with manual aspirators and placed in holding cages with glucose as a food source. The number of recaptured mosquitoes was recorded for each experiment.

The number of *Culex* egg rafts in each In2Care® Mosquito Trap and ovipot were recorded upon retrieval to assess if there was a breeding preference for any of the sites. To assess the larvicidal impact of the pyriproxyfen in the In2Mix®, 20 L3-stage *Culex* larvae were added to each In2Care® Mosquito Trap and each ovipot upon retrieval. Adult emergence rates were monitored as described below.

Measuring adult emergence inhibition: Traps and ovipots were collected from the semi-field cages and their contents were transferred into separate labeled, clean glass bowls that were kept in a laboratory room. Five mL

of a liver powder and Brewer's yeast slurry was added to each bowl as a larval food source, and a nylon stocking was placed over each bowl to capture any emerging mosquitoes. Bowls were checked daily for a maximum of 14 days, after which all pupae had died, or all adults had emerged. The total number of emerged adult *Culex* mosquitoes (from the 20 added *Culex* larvae) and the number of dead larvae and pupae were recorded for each bowl.

The adult emergence rates (% *Culex* adult mosquitoes developed from the 20 added larvae) were used as a proxy for the larvicidal impact of the pyriproxyfen in the In2Mix®. Pyriproxyfen autodissemination was determined by comparing the mean percent adult emergence in the ovipots placed around the In2Care® Mosquito Trap in the test replicates to the mean percent adult emergence from the ovipots in the control replicates.

Mosquito bioassays for fungus assessments: Due to extreme variability and insufficient mosquito recapture (average of only 30% recaptured) rates in the semi-field environments, In2Mix® fungus was tested against adult *Cx. quinquefasciatus* females in plastic tubes (125 mm length, 44 mm diameter, 16-mesh gauze at either end) that were held in a side-chamber of the semi-field cage. Twenty-five *Cx. quinquefasciatus* adult females were exposed for 3 minutes in a tube, transferred to a clean holding cage with 10% sucrose available, and placed in the side chamber where temperature and humidity was recorded with data loggers. Five replicates were conducted where the mosquitoes were monitored daily for 14 days, after which all of the experimental mosquitoes had died from *Beauveria bassiana*.

Statistical analyses: Statistical analyses were done using SPSS 26.0 software. Normality of the data was investigated using the Shapiro-Wilk test. Homogeneity of variances was tested with Levene's test. Comparisons of egg raft collections between control and test replicates were performed using independent sample T-tests for normally distributed data and Kruskal-Wallis (Mann-Whitney U) tests for data that was non-normal and had unequal variances. Analyses of larvicidal impacts were performed using a one-way ANOVA test followed by a Tukey post-hoc test.

For adulticidal impact assessments, a Kaplan-Meier pair-wise analysis was used with the log-rank test in SPSS to compute survival functions from the nonparametric life-time data, and to test the null hypothesis that survival functions did not differ across the pooled replicates of the control and test groups. Kaplan-Meier test statistic results were compared with a Chi-squared distribution with one degree of freedom to yield a P-value.

(3) **Results:** Mosquito recapture was a significant confounding issue for the semi-field testing. On average, only 30% of the released mosquitoes were recaptured in the test replicates. Therefore, retrieved mosquito groups were not monitored for survival. Instead, mosquito bioassays were conducted to assess adulticidal impacts across the experimental groups while 75% were recaptured across the controls.

Attractiveness of the In2Care® Mosquito Trap: In the control replicates, an average of 21 egg rafts were deposited in total by on average 41% of the released gravid *Culex* mosquitoes. The Test replicates with an In2Mix®-baited In2Care® Trap showed an equal mosquito breeding success; 49% of mosquitoes had laid eggs (22 egg rafts on average).

In the control experiments there was an equal egg raft distribution over the 5 ovipots. In the test replicates, however, on average 17 ± 2% of the egg rafts were laid per ovipot and 35 ± 4% of all eggs were laid inside the In2Mix®-treated In2Care® Trap (Fig. 1). This significantly higher egg-laying proportion ($P<0.05$) indicated that the traps were more attractive to container-breeding *Cx. quinquefasciatus* than the alternative ovipot breeding sites and confirmed that presence of the In2Mix® biocide powders does not negatively affect the attraction to mosquitoes.

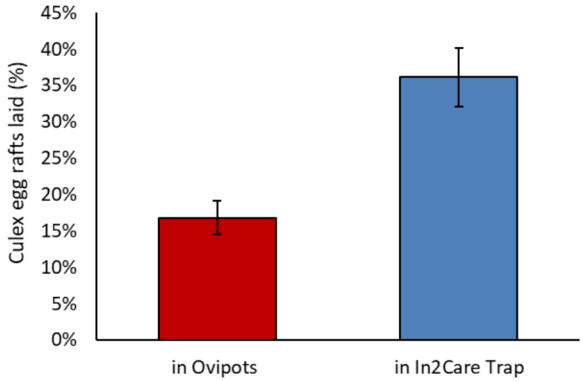

Figure 1. *Cx. quinquefasciatus* egg distribution in ovipots and in In2Care® Traps.

Larvicidal impacts of In2Care® Mosquito Traps: Baseline mosquito emergence results showed that in the clean control replicates, on average 87.3 ± 1.8% of the added larvae fully developed and emerged as adult *Culex* mosquitoes. In contrast, in the In2Mix®-baited In2Care® Traps, 0% adult emergence was observed for all replicates (Fig. 2). All *Culex* larvae were killed in the late L4 stage or pupal stage, and dead pupae showed a recognizable black color and de-curling of the tail which is distinct for pyriproxyfen-induced molting inhibition. The registrant submitted pictures of dead larvae, but actual larvae and pupal mortality data was not submitted. There was 100% adult emergence inhibition which confirmed that the In2Mix® in the In2Care® Mosquito Traps effectively killed all *Culex* larvae and can act as an egg sink to fully prevent adult emergence of progeny from eggs deposited by visiting females.

Autodissemination impacts: Results also confirmed successful pyriproxyfen autodissemination by wild-type *Culex quinquefasciatus* mosquitoes under ambient climate conditions. On average, adult emergence rates from added larvae were 55.5 ± 6.5% in the ovipots placed around the In2Care® Mosquito Trap in the test replicates. This proportion of adult mosquito emergence was significantly lower than the 87.3 ± 1.8 % baseline *Culex* emergence observed in the control ovipots (P<0.001; Fig. 2). The observed pyriproxyfen-specific larvicidal/pupacidal effect confirmed that the pyriproxyfen was successfully spread by the mosquitoes (autodisseminated) from the In2Care® Trap to the ovipots and reduced the breeding success of the *Culex* mosquitoes.

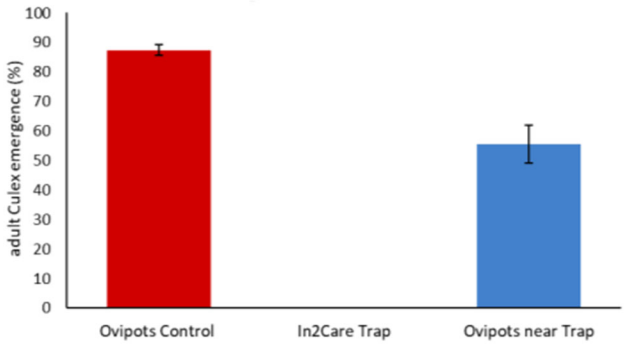

Figure 2. *Culex* adult emergence rates from added larvae.

Adulticidal impacts: Bioassay results showed that mosquito survivorship was significantly reduced after exposure to In2Mix® containing *B. bassiana* spores (Fig. 3). The survival curves of In2Mix®-exposed cohorts showed a sigmoid decline that is typical of *Beauveria*-induced lethality, killing the majority of the mosquitoes within 9 days and all *Culex* females within 13 days. Control group survival was still 94% on average at 13 days post-exposure. Kaplan-Meier analyses confirmed that the observed differences between the survival curves of the control and test cohorts were highly significant (P<0.001).

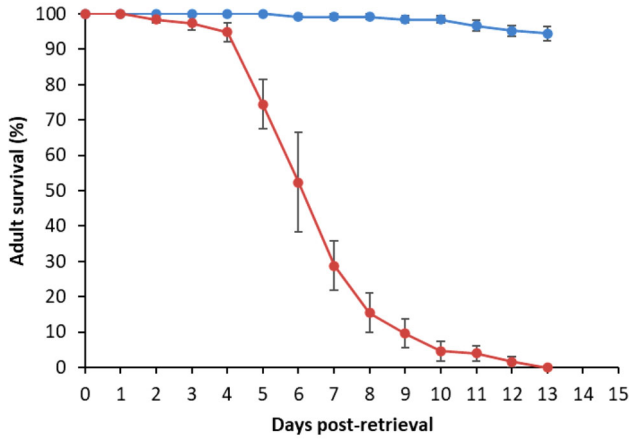

Figure 3. Adult *Cx. quinquefasciatus* survival.

(4) **Conclusion: Partially acceptable.** The rate tested was more than the minimum labeled rate of 1 trap per 4300 ft^2 (400 m^2). The study demonstrates that the product:

- Prevents *Culex* adult emergence for up to 13 days.
- Attracts *Culex* adult females.

Kills claims for adult *Cx. quinquefasciatus* are not supported by this data as 90% mortality didn't occur until 9 days post-exposure. To support kill claims of adult mosquitoes, acceptable mortality data (≥90% mortality) within 96 hours should be provided). Control claims are not supported. To obtain control claims minimum of 90-95% population reduction, based on pre-and post-treatment infestation counts from attest conducted under field conditions is required. Kills claims for larvae are not supported by this data. No data was provided that demonstrated larval or pupal mortality and the only endpoint that was reported was successful or unsuccessful adult emergence. Larvae-specific data must be presented for larvicidal claims. The registrant suggested that adult emergence be used as a proxy for larvicidal impact, but these are two separate life stages that should be evaluated and classified separately.

Although the Agency has accepted semi-field studies for these types of products, field studies are preferred. Some issues that we have seen with semi-field studies are the inability to test the lowest label rate and low levels of recapture. While the adult exposure to *Beauveria bassiana* became a forced exposure assay, the tubes the mosquitoes were placed in were kept in the semi-field environment after treatment. It could be argued that this does not replicate field conditions since the mosquitoes did not interact with the fungi naturally, but since it was demonstrated that the trap is attractive to gravid females and autodissemination was established in a separate assay, it is reasonable to conclude that the female mosquitoes would make contact with the fungi within the trap. The flaws that led to undesirable recapture rates were more closely associated with experimental design and not the efficacy of the trap itself. Since the treated mosquitoes were placed in the semi-field environment, they were still held at the outdoor environmental conditions that were necessary to demonstrate efficacy in addition to lab data that was supplied in a separate study. Also, it is possible that low efficacy could be due to environmental conditions not being optimal for *B. bassiana* during the semi-field study.
Data do not support auto-dissemination claims from female Culex to nearby breeding sites. Adult prevention of emergence was >55% and a much higher labeled rate was tested.
Future studies should be conducted in the field and test the minimum labeled rate.

Study #3: *Aedes* and *Culex* Field Tests (San Bernardino County, California)

(1) **GLP:** non-GLP

(2) **Methods:** The objectives of the study were to demonstrate that In2Care® Mosquito Traps (baited with In2Mix®) attract and kill *Aedes* and *Culex* mosquitoes in a field setting.

Trap deployment and servicing: In this field study 326 In2Care® Traps were deployed in *Aedes*-infested neighborhoods in 6 cities across the West Valley Mosquito and Vector Control District (MVCD) in Ontario, California, USA. The operation was implemented in stepped phases between 4/26/19 and 10/25/19 at a concentration of approximately 1 trap per yard (i.e., 326 traps at 305 different homes) and traps were reloaded and maintained every 4 weeks for the duration of the study. Traps were distributed over an area of 544 km^2 as shown in Fig.1. The registrant tested a lower rate than the minimum labeled rate and traps were placed at a lower density than recommended on the label due to limited resources (average dispersion density was 1 trap per 6550-7950 ft^2 versus the label rate of 1 trap per 4300 ft^2). Against the advice of the manufacturer, traps were not relocated if there was no positive mosquito breeding observed at a given site. Traps were placed at a lower density than the label rate due to limited resources and no outdoor environmental data was provided for the study area during the 6-month testing period.

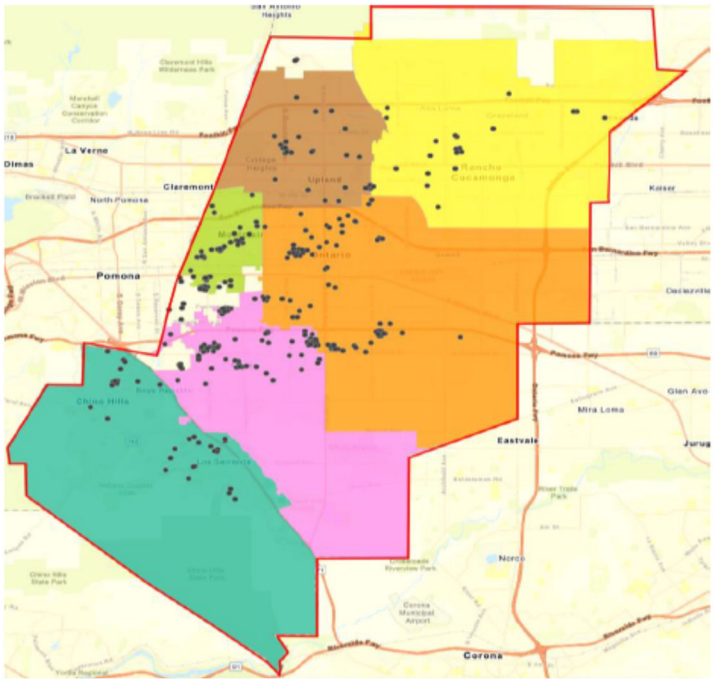

Figure 1. In2Mix®-baited In2Care® Trap distribution across MVCD in Ontario, California.

When setting up the traps, the In2Mix® sachet containing the biocides, odor tablets, and gauze was shaken well to maximize the attachment of biocides to the gauze. The remaining biocide powder was sprinkled into 3.8 liters of tap water inside the reservoir. During servicing, the reservoirs were emptied and rinsed with tap water, removing the remaining biocides, debris, and sediment. Each reservoir was refilled with the same amount of tap water and a new sachet was applied as described previously. Traps were replenished every 4 weeks per product label instructions (In2Care 2020).

Profile of larval breeding in In2Care® Mosquito Traps: A no-choice test was performed. Upon retrieval, contents of the traps (including up to 250 mL of water) were transferred to 480 mL clear plastic containers with a snap lid and slit for ventilation and brought back to the laboratory for further analysis. 1st through 4th instars were counted, but only 3rd and 4th instars were identified to species.

Inhibition of emergence in collected larvae and pupae: Collection containers that held mainly late-stage larvae and pupae and slight to moderate amounts of organic matter were selected to observe for adult pre-emergence. All larval life stages found in the traps were counted and recorded. Subsamples of 2-3 1st and 2nd instars were killed with 95% ethanol and identified as *Culex* or *Aedes* (no other identifiable genera observed). 3rd and 4th instars were counted, identified to species, and then observed daily for pupation and/or adult emergence until no

late-stage instars or pupae remained. Adult emergence was checked daily, and observations were concluded when no more surviving late instars or pupae were present in the cup. Successful adult emergence was defined as any adult completely separated from its pupal exuvium.

Residual trap activity on inhibition of adult emergence: Residual pesticidal activity was tested where 2-3 traps that had been out in the field were brought back to the laboratory. 3.8 L of tap water was added to a single reservoir and two 1-day-old egg rafts from a susceptible *Cx. quinquefasciatus* laboratory colony were added along with rabbit pellets to feed the larvae. The larvae were monitored daily for growth, pupation, and mortality and viable pupae were transferred to separate Styrofoam cups containing 120 mL of water to check for adult emergence. Percent adult emergence was calculated using the following formula:

$$\% \text{ IE} = 100 \text{ x } [\text{number of pupae} - \text{number of exuviae}] / \text{number of pupae}$$

Three new and clean In2Care® Mosquito Trap reservoirs that were never used in the field, and did not supposedly have any activity of pyriproxyfen, were used as controls in laboratory bioassay. These laboratory studies were carried out in an insectary held at 27.8-28.9°C, 40-60% RH, and a 10 L:14D photoperiod. No statistical analyses, including statistical tests used and raw data, were provided.

(3) **Results:**

Profile of larval breeding in In2Care® Mosquito Traps: 105 (32.2%) of the 326 traps that were deployed contained immature mosquitoes with each hosting an average of 5 *Aedes aegypti* and 25 *Culex quinquefasciatus* (Table 1). Five traps (1.5%) had early instars and/or pupae only, which could not be identified. Overall, early instars were present in 38 traps (17.5 larvae/trap), and pupae were detected in 40 traps (8.9 pupae/trap). Three collections with mixed *Culex* and *Aedes* larvae were not counted because of heavy organic content and were excluded from larval density counts. It is possible that such a low number of traps contained mosquito larvae due to climatic conditions at the time of the study and the failure to relocate traps that were placed in locations where no positive mosquito breeding was observed.

Table 1. Presence and distribution of immature mosquitoes in 102 traps collected (2019).

Species/stages	*Aedes aegypti* only	*Culex quinqefasiatus* only	*Aedes aegypti* & *Culex quinq* [2]	Early instars	Pupae	Total
No. Positive traps	37	39	21	38	40	102
Avg. no./Trap ± SE	8.8 ± 1.3	47.1 ± 7.2	5.0 ± 0.9 25.0 ± 5.3	17.5 ± 3.5	8.9 ± 1.3	37.4 ± 3.9

[1] 326 In2Care traps were set and retrieved from April 26 to November 21, 2019. There were no other species present in the samples based on identifiable larvae.

Inhibition of emergence in collected larvae and pupae: Fourteen collections were further analyzed to observe adult emergence. No adults emerged (0% emergence; 100% inhibition) from the late-stage larvae and pupae collected from these containers as shown in Table 2.

Table 2. Adult emergence from 14 baited traps subsampled from 3 cities in CA.

	Fourth instars		
	Aedes aegypti	*Culex quinquefasciatus*	Pupae
No. Observed	79	7	160
% adults emerged	0	0	0

[1] Larvae and pupae for IE% observation were made from 14 traps in 3 cities. Mortality occurred at larvae, during transition from larvae to pupae, or at pupae. There was no incomplete adult emergence noticed.

Bioassays on residual activity of inhibition of adult emergence in In2Care® Mosquito Traps: Laboratory

bioassays were conducted to examine residual activity of previously deployed traps. The In2Care® Mosquito Traps (16 of them) had been deployed in the field and refilled 0-6 times before recovery. Table 3 shows that no adults (0%) emerged from traps that spent 27-200 days in the field, while 305 adults emerged from unused and untreated traps (average from 3 unused traps).

Table 3. Residual activity of field-used traps.

Sachet refills	Trap in the field (days)	First round			Second round		
		Pupae collected	Adults emerged	% IE ± SE	Pupae collected	Adults emerged	% IE ± SE
Unused reservoir	n/a	322	305	5.3 ± 1.2	315	311	1.3 ± 0.6
0	27-28	242	0	100	98	0	100
1	54-57	136	0	100	258	0	100
2	85	53	0	100	100	0	100
3	113	1	0	100	104	0	100
4	137	1	0	100	0	0	100
6	200	365	0	100	309	0	100

The mortality in the untreated controls remained low, 5.3% and 1.3% out of 322 and 315 pupae, respectively, for each test series. Introduced egg rafts in each trap reservoir hatched normally, as indicated by the presence of live newly hatched larvae. However, progressive mortality of immature mosquitoes occurred at the following stages: early and late larvae, transitions from larvae to pupae (‘‘puparvae’’), or pupae. Actual dead larvae counts were not submitted.

(4) **Conclusion: Partially acceptable**. Although the rate tested was lower than the labeled rate of 1 trap per 4300 ft^2, acceptable data from this field study could be bridged to the minimum labeled rate and it does not appear that the lower density significantly influenced efficacy. The Agency understands the constraints of finding houses/backyards close enough to one another to perform this type of experiment. The data supports that *Aedes* and *Culex* mosquitoes were found breeding in the In2Care® Mosquito Traps and the treated traps prevented adult emergence for 4 weeks. However, the data did not support attractancy claims for these species. A choice test between In2Care® Mosquito Traps and alternative oviposition sites should be performed to obtain attractancy claims.

Kills claims for larvae are not supported by this data since no larval mortality data was reported. The registrant only measured counts of collected pupae and emerged adults. Percent adult emergence cannot be used as a proxy for larvicidal efficacy. Kills claims for adult mosquitoes are also not supported as adult mortality was not measured in this study and mosquitoes were dying in the larval or pupal stage. Larval/pupal controls claims are unsupported since no clear data was presented that quantified how long larvae and pupae had been in the traps and/or how long it took them to die.

Control claims are not supported. Traps were replenished every 4 weeks. Traps were placed in the field for different times and refilled at different times (0-7 times). Aged sachets. as previously recommended to the registrant, were not tested.

Study #4: *Aedes* Large-Scale Field Test (Manatee County, Florida)

Conclusion: Extraneous submission. This study is not applicable to this submission as it contains a comparative field data between the In2Care® trap and a combination of several Integrated Vector Management (IVM) tactics. The Agency does not review comparative data. Testing must be product-specific and a minimum of 95% population reduction must be observed, based on pre- and post-treatment infestation counts from tests conducted under field conditions. Thus, these data will not be reviewed here.

Study #5: *Aedes* Field Test (Bangkok, Thailand)

(1) **GLP:** non-GLP

(2) **Methods:** The objectives of the study were to assess the larvicidal and autodissemination impacts of In2Mix®-baited In2Care® Mosquito Traps, with a 6-week servicing interval, against field populations of *Aedes aegypti* mosquitoes. Additionally, the study contains user satisfaction surveys data. For the purposes of this review, only trap efficacy data will be reviewed.

Trial location: A 3-month trial was carried out in which 33 In2Care® Mosquito Traps were distributed over a 4-acre site (1 trap/5280 $ft.^2$) on the grounds of a learning institute in Bangkok, Thailand. Note: the current label states that 1 trap every 4,300 $ft.^2$ (400 m^2) is suggested for "optimal coverage."

In2Care® Mosquito Trap Experiments: Experiments used the black plastic In2Care® Mosquito Traps and In2Mix® sachets containing 74.03% pyriproxyfen and 10% *Beauveria bassiana* strain GHA as active ingredients. In2Care® Traps were treated with In2Mix® on the first day of the experiment following the Directions For Use (DFU) on the label. Each Trap was filled with 4.5 L of clean tap water and the In2Mix®-treated netting strip was taken out of the refill sachet and attached to the floater. The floater was then gently placed on the water surface. The remaining In2Mix® powder and the 2 yeast tablets from the refill sachet were added to the trap water. *Aedes* egg and larvae counts were made for all 33 traps every 2 weeks and over the course of the experiment all of the In2Care® traps were serviced once at 6 weeks where a new refill sachet and clean water was introduced.

Measuring adult emergence inhibition:
5 ovitraps (untreated traps; separate from the 33 treated traps) we placed in random locations across the 4-acre site to assess autodissemination of active ingredients from the baited traps. Their water contents were collected every 2 weeks and transferred to clean plastic cups in the laboratory to test for larvicide autodissemination. 50 laboratory-reared *Aedes* larvae (it is unclear what instar) were added to the ovitrap water and adult emergence rates were monitored to assess pyriproxyfen presence. There is a discrepancy with the raw data table on page 68 of the report, where it is stated that 20 larvae were added per mosquito sample. For the purposes of this review, the reviewer will consider the raw data. Additional larval food and a nylon stocking was placed over each bowl to capture any emerging mosquitoes. Cups were checked daily until all pupae had died or all adults had emerged.

The total number of emerged adult *Aedes* mosquitoes (from the 50 added *Aedes* larvae) and the number of dead larvae and pupae were recorded for each cup. The adult emergence rates (% *Aedes* mosquitoes developed from the 50 added larvae) were used as a proxy for the larvicidal impact of the (pyriproxyfen in the) In2Mix®. Pyriproxyfen autodissemination was determined by comparing the percent adult emergence in the ovitraps placed around the In2Care® Mosquito Trap in the field area to the percent adult emergence from control cups. Environmental conditions (temperature, humidity, precipitation, etc.) at the study site were not provided. Mosquito pressure before the traps were distributed (including different mosquito species observed) or untreated control data collected prior to treated trap deployment was not reported. Distance between In2Care® Mosquito Traps and distance from In2Care® Mosquito Traps to untreated ovitraps was not provided. Pesticide exposure history and rearing conditions of lab-reared mosquitoes used in laboratory bioassays was not described. It is unclear if traps were new or cleaned before the experiment and considered insecticide-free. Statistical justification for several factors including the number of treated and untreated traps deployed was not provided.

(3) **Results:** The number of eggs and larvae found in the 33 In2Care® Mosquito Traps that were deployed between November 2019 and February 2020 is displayed in Fig. 1 and Table 1. Over the 12 weeks of the study, we see a reduction trend in both the number of eggs and larvae present in the traps. However, there appears to be no replication since the values were pooled and there are no visible error bars on the chart, standard deviations on the table, or explanation of any statistical analyses. It is also clear that no baseline values were established before the active ingredients (in the In2Mix® sachets) were deployed to indicate the magnitude of mosquito pressure pre-treatment. Therefore, the reviewer cannot determine if statistically significant reduction occurred based on what was presented that would have an impact on the overall mosquito numbers in that area. There was also no description of how the different mosquito life stages were identified to genus and/or species.

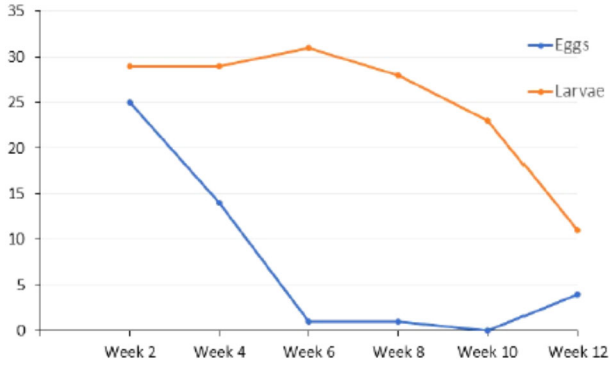

Figure 1. *Aedes* egg and larvae counts (pooled data from 33 In2Care® Mosquito Traps).

Table 1. Number of traps containing mosquito eggs and/or larvae (n=33).

What	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
Eggs and/or larvae	29	29	31	28	23	11
Eggs	25	14	1	1	0	4
Larvae	29	29	31	28	23	11

The percent adult emergence trends downward as shown in Table 2, Table 3, and Fig. 2. However, there is a lack of detail concerning trap subsampling, calculations, and statistical analysis that makes these observations unreliable. Also, it looks as though directly after the trap maintenance and sachet refilling at week 6 occurred there was complete inhibition of adult emergence. This may be due to exposure of more than the label amount of active ingredients (bioaccumulation) as earlier studies showed that the trap retains activity after more than one treatment with the In2Mix® powder.

Table 2: Adult mosquito emergence inhibition from treated traps (5 of 33 treated traps subsampled).

Emergence inhibition in water collected from In2Care Mosquito Traps. 20 larvae were added per Mosquito Trap water sample. Number of emergenced adults are shown.		
Trap No.	Adult Mosquito Week 6	Adult Mosquito Week 12
15	0	0
25	0	0
27	0	0
30	0	0
31	0	0
Average	**0**	**0**

Table 3: Percent adult mosquito emergence from untreated ovitraps.

Emergence inhibition in water collected from ovitraps 50 larvae were added per ovitrap. Percentage shows the emergence inhibition (mortality)						
Ovi-Trap No.	Adult Mosquito Week 2	Adult Mosquito Week 4	Adult Mosquito Week 6	Adult Mosquito Week 8	Adult Mosquito Week 10	Adult Mosquito Week 12
4	74%	78%	100%	100%	100%	100%
5	56%	72%	92%	100%	100%	100%
9	44%	96%	100%	100%	100%	100%
25	34%	86%	100%	100%	100%	100%
28	36%	76%	90%	100%	100%	100%
Average	**49%**	**82%**	**96%**	**100%**	**100%**	**100%**

50 larvae added to sampled Ovitraps (N=5)

	% adult emergence	
Week 2	51	
Week 4	18	
Week 6	4	
Week 8	0	*PPF-induced kill of Aedes pupae*
Week 10	0	*→ no adult mosquitoes formed*
Week 12	0	

Figure 2: Pyriproxyfen dissemination test.

(4) **Conclusions: Unacceptable**. The data submitted do not support the prevention of *Aedes* adult emergence in treated traps for up to 12 weeks. Prevention of emergence was not acceptable at weeks 2 or 4. To support prevention of emergence claims, acceptable data (≥90% prevention of emergence) at all time points should be provided. Additionally, the data does not support autodissemination claims, because the prevention of adult emergence observed in collected ovitrap water was not ≥90% at all data points. Future studies should contain acceptable efficacy data at all data points. Despite a perceived reduction in the number of eggs laid and larvae present, in the treated traps, there is insufficient evidence to support larvicidal effects. Also, a lack of detail on experimental design and execution makes it impossible for the reviewer to support said findings.

Population reduction claims are not supported for Aedes mosquitoes. For population reduction-type of claims, an experimental design including (a) assessment of what is considered "residual activity" of the product and (b) 'pre' and 'post' assessments of mosquito populations from the surrounding area of the test site that use currently accepted standards (e.g., sweeps or the CDC trap), preferably those that do not rely on traditional landing counts in light of the potential risk for mosquito-borne disease transmission. Also, environmental conditions must be reported as adverse parameters could have an effect on the study's outcome. It is unclear if the ovitraps were brand new or had been used in previous studies. The data suggests that at some point the active ingredients are binding to the product (bioaccumulation) and adding new sachets every 4 weeks is producing an additive effect where the dosage is higher than what is on the product's label. Consumer survey data was not reviewed and cannot be used to conclude that there was mosquito population reduction.

Study #6: *Aedes* Field Test (Vientiane, Lao PDR)

(1) **GLP:** non-GLP

(2) **Methods:** The objective of the study was to test the residual efficacy of In2Care® Mosquito Traps under tropical climate conditions in Laos against wild-type *Aedes* vectors to determine if the servicing timeframe could be extended beyond the current 4 weeks servicing interval.

20 In2Care® Mosquito Traps were distributed over a 3.2-acre site at a concentration of 1 trap/648 m^2 (less than the minimum labeled rate) in Vientiane, Lao PDR where there is a tropical climate and distinct dry and wet seasons annually. The baited traps were evaluated from January to April of 2018 during the dry season and again from July to October during the wet season. Pre-test and post-test evaluations of *A. aegypti* numbers in the area were conducted from January to December of 2017 and 2019, respectively. The traps in the experimental portions of the study were baited with In2Mix® sachets containing 74.03% pyriproxyfen and 10% *Beauveria bassiana* only on the first day of the experiment (i.e., no refills).

Mosquitoes: A laboratory strain of *A. aegypti* was established from field-caught larvae and pupae collected from the Sisattanak district of Vientiane capital in Kao-gnot village (17.962684°N, 102.615035°E). They were reared indoors under normal conditions at 27 (±2)°C and 80 (±10)% relative humidity and their progeny were made available for laboratory testing.

Water level and mosquito attraction: 20 In2Care® Mosquito Traps (baited) were deployed over 12 weeks in the dry season and 12 weeks in the wet season of 2018. Each trap was baited with a single In2Mix® sachet on the

first day of the experiment and monitored at 4, 6, 8, 10, and 12 weeks post-deployment without adding any additional bait. The water levels were measured at each observation time and the traps were topped off with additional water as necessary. At those same observation points the number of *A. aegypti* larvae were counted in each trap to evaluate attraction. No choice tests, including alternate oviposition sites were performed.

Larvicidal efficacy: At 4, 6, 8, 10, and 12 weeks post-deployment, four traps were randomly selected and 250 mL of water from each trap was collected (which contained any larvae present) and transferred to breeding cups. If there were no larvae present, the water from the trap was collected and 25 L_3 lab-reared larvae were added. Adult emergence was monitored for the treated samples and separate untreated control samples.

Mosquito monitoring: In the pre- and post-deployment phases adult and larval *A. aegypti* were monitored with 2 BG sentinel traps (for adult capture) and 2 untreated ovitraps (for larval) capture that were placed in the test area and monitored weekly. Captured adult mosquitoes were identified to species and counted, and adult emergence from collected larvae was evaluated as described above.

Statistical analysis: The mosquito surveillance data was collected with two ovitraps and two BG traps from January 2017 until December 2019. The data of both trial periods collected in 2018 was compared with the data in the same months in 2017 and 2019 and analyzed with an ANOVA with Tukey post-hoc analysis in R (R Development Core Team, 2020) using the "car" package. For all statistical analyses, the significant P-value was set at 0.05 or less.

(3) **Results:** This study was designed to measure the efficacy of pyriproxyfen (larvicide) for up to 12 weeks post-deployment on *Aedes aegypti* and examine potential autodissemination to surrounding breeding sites. It was also conducted to evaluate water levels in the traps to determine how often they needed to be refilled if necessary.

Trap water levels: The temperature and relative humidity at the test site during the dry season (January to April, 2018) were 25.9 (±4.7)°C and 62.6 (±13.8)%, respectively. The temperature and relative humidity at the test site during the wet season (July to October, 2018) were not measured, but average weather data in the region for temperature and relative humidity was 27.7°C and 83%, respectively. Fig. 1 shows that no water refills were needed during the 12-week test period of the wet season for any of the 20 traps deployed. 3 traps dried out by week 4 and 2 others by week 6 in the dry season (out of 20 total).

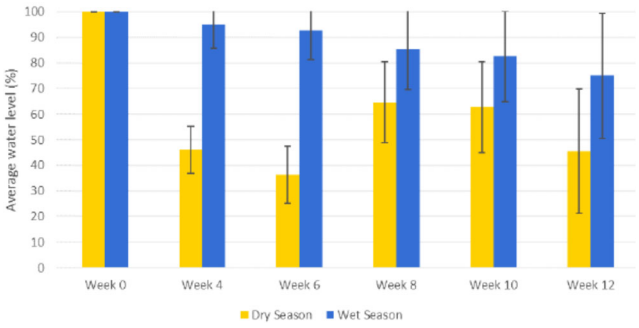

Figure 1. Water level 0, 4, 6, 8, 10, and 12 weeks after intervention in the dry season (yellow) and the wet season (blue) at the test site in Vientiane, Lao PDR.

Mosquito attraction test: Fig. 2 shows the number of larvae that were collected from the traps in the wet and dry seasons. There was no statically significant difference in the number of larvae found in traps for the duration of the study in either the wet or dry season.

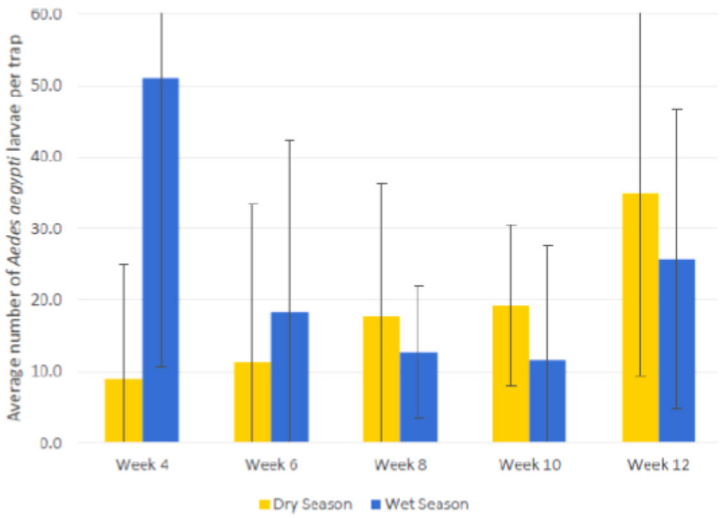

Figure 2. *A. aegypti* larvae collected 4, 6, 8, 10, and 12 weeks after intervention in the dry season (yellow) and the wet season (blue) at the test site in Vientiane, Lao PDR.

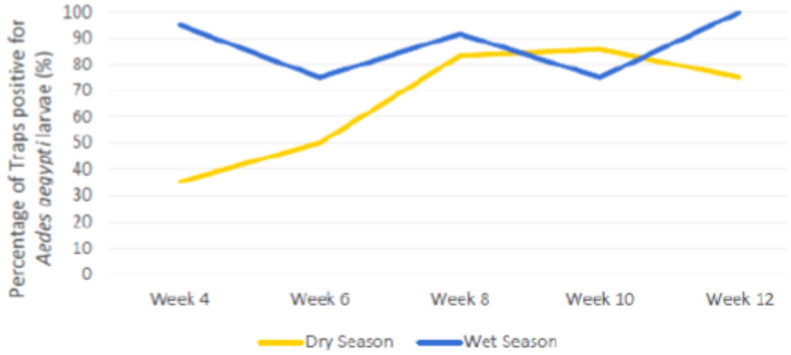

Figure 3. Percentage of traps positive for *A. aegypti* larvae collected 4, 6, 8, 10, and 12 weeks after intervention in the dry season (yellow) and the wet season (blue) at the test site in Vientiane, Lao PDR.

Larvicidal efficacy test: Table 1 and Fig. 4 show that adult emergence was completely prevented (0% adult emergence) at 4, 6, 8, 10, and 12 weeks post trap deployment in both the dry and wet season (2018) while an average of ≥89.6% adult emergence was observed in controls from 2017 and 2019 (raw data not provided). Only 80-88% control adult emergence was observed and no justification of what happened to the other 20% larvae was provided.

Table 1. Percentage of mosquitoes emerged from larvae collected from field traps (i.e., 4 traps randomly selected). Note: if no mosquitoes were in trap, laboratory reared specimens were substituted.

	Dry Season		Wet Season		Control	
	Percentage Mosquitoes emerged	N	Percentage Mosquitoes emerged	N	Percentage Mosquitoes emerged	N
Week 4	0 %	101	0 %	145	92 %	25
Week 6	0 %	77	0 %	83	100 %	25
Week 8	0 %	94	0 %	11	96 %	25
Week 10	0 %	102	0 %	49	80 %	25
Week 12	0 %	165	0 %	88	88 %	25

Table 2 and Fig. 4 show adult emergence from larvae collected during the test and control phases of the experiment. This data supports prevention of adult emergence during both the wet and dry seasons.

Table 2. Average number of *A. aegypti* adults emerged from larvae collected from traps in the wet season (2018), dry season (2018), and control (2017 and 2019) traps.

	2017 (Control)	2018 (Intervention)	2019 (Control)	P -value (Intervention vs Control)
Dry Season (January - April)	34.2 ± 20.3 [a]	0.0 ± 0.0 [b]	21.9 ± 31.5 [ab]	0.0467
Wet Season (July – October)	9.5 ± 10.5 [a]	0.0 ± 0.0 [b]	33.0 ± 35.8 [a]	0.0469

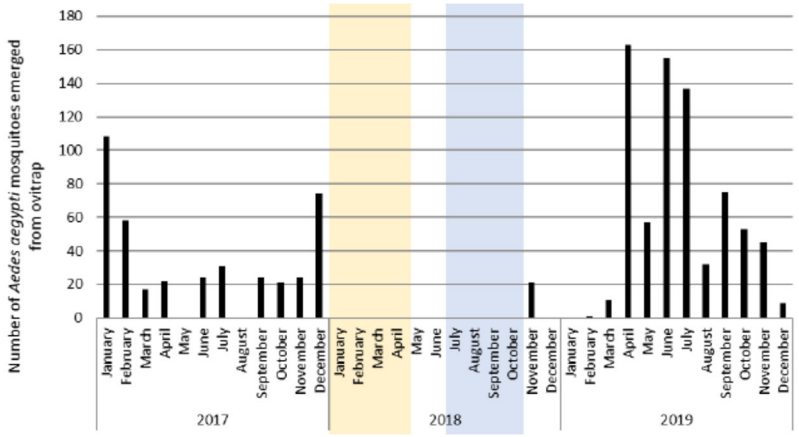

Figure 4. Monthly breakdown of *A. aegypti* adult emergence from larvae collected from traps in wet season (2018), dry season (2018), and control (2017 and 2019) traps.

Table 3 and Fig. 5 shows the number of *A. aegypti* adults captured by BG Sentinel traps in the test area over the course of the study (2017-2019). This data shows that no significant differences were found in the number of adults captured between the control and test portions of the experiment. In addition, no data was supplied that supports autodissemination of the active ingredient(s).

Table 3. Average number of adult *A. aegypti* captured from 2017-2019 in test area.

	2017	2018	2019	P -value
Dry Season (January - April)	0.0±0.0	0.3±0.5	0.3±0.5	0.585
Wet Season (July – October)	2.4±2.2	0.9±0.8	1.7±1.8	0.211

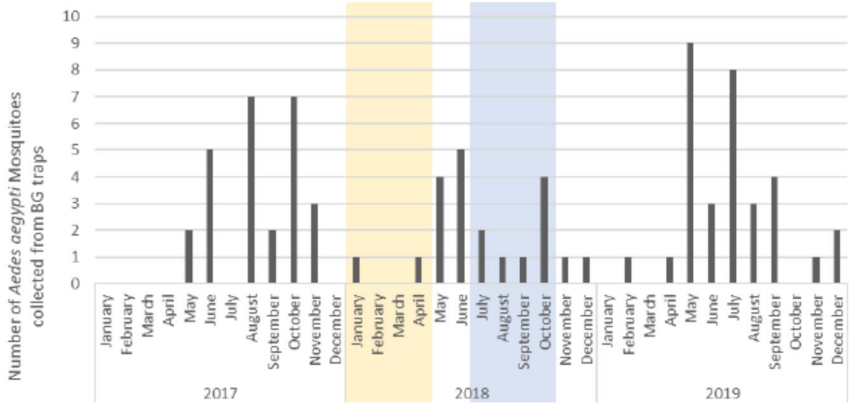

Figure 5. Monthly breakdown of *A. aegypti* adults captured from 2017-2019 in test area.

(4) **Conclusion: Partially Acceptable**. The rate tested is less than the minimum labeled rate. However, the tested rate can be bridged to the minimum labeled rate of 1 trap per 4300 ft^2. Data support claims that the product prevents emergence of adult *Aedes* mosquitoes for up to 8 weeks. Kill/control claims for adult mosquitoes are not supported. A minimum of 90-95% reduction, based on pre-and post-treatment infestation counts should be demonstrated, ideally during the same season.

The study claims that all larvae collected during subsampling from the baited/treated traps were killed by pyriproxyfen. However, percent adult emergence was used as a proxy for larval mortality. No larvae-specific mortality data was provided to support larvicidal claims. Therefore, the only claim that can be justified by this data is that adult emergence was prevented.

Population reduction claims are not supported. Population reduction claims are not supported for Aedes mosquitoes. For population reduction-type of claims, an experimental design including (a) assessment of what is considered "residual activity" of the product and (b) 'pre' and 'post' assessments of mosquito populations from the surrounding area of the test site that use currently accepted standards (e.g., sweeps or the CDC trap), preferably those that do not rely on traditional landing counts in light of the potential risk for mosquito-borne disease transmission.

Attraction was not demonstrated in this study. Attraction suggests a preference for the breeding site within the trap over other alternate oviposition sites. The data presented only shows that *Aedes* mosquitoes were breeding in the traps in the dry and wet season (no statistical difference since error bars overlap). No choice tests comparing numbers of mosquitoes visiting/breeding the treated traps, vs and alternate breeding site were performed. For *Culex* mosquitoes only cage and semi-field data showed attraction of the traps for this species. However, this was not corroborated with field data in a choice test.

IV. EXECUTIVE DATA SUMMARY:

MRID 51615606 is **partially acceptable**. Data submitted demonstrates that when one Ln2Care trap is deployed at the minimum labeled rate of 1 trap/4300 ft^2it prevents emergence of adult *Culex* mosquitoes for up to 4 weeks and adult *Aedes* mosquitoes for up to 8 weeks. Both, *Aedes* and *Culex* mosquitoes are found breeding in the Ln2Care traps. Kill/control clams for *Aedes* or *Culex* adults, larvae or pupae are not supported, as mortality was either not assessed or unacceptable.

Cage and semi-field studies (neither of them tested the minimum labeled rate) support that *Culex* adult females auto-disseminate larvicide to their breeding sites and the trap attracts *Culex* adult females. However, this was not corroborated with field data. A similar situation was observed with attraction studies, where there was no acceptable field data to support these claims. Attraction claims are not supported for *Aedes* mosquitoes either.

Although traps were tested for 12 weeks in the field, the submitted data were not adequate to determine duration of efficacy for the proposed sachet, therefore a 4 week replacement interval for sachets remains. For longer replacement intervals, data will need to be submitted showing efficacy of aged sachets.

Field data testing the minimum labeled rate and appropriate efficacy endpoints are recommended.

V. LABEL RECOMMENDATIONS:

(1) Make the following changes in the Directions for Use:

- Kills/controls for *Culex*, larvae or adults are not supported.
- Expansion of longevity of the trap from 4 to 6 weeks is not supported. Although prevention of adult Aedes emergence is for up to 8 weeks, because the registrant intends to use the traps for both species and traps will need to be refilled sooner for Culex, 4 weeks is the limiting factor. Furthermore, kills/control claims for *Aedes* mosquitoes were not supported by the data submitted.

(2) The following marketing claims are acceptable:

- Kills [disease carrying mosquitoes that may transmit [Zika virus]

(3) The following marketing claims are unacceptable (other unacceptable claims are indicated in the label):

- Residual control that lasts up to 6 weeks.
- General kills/controls mosquito claims.
- Controls container-breeding Culex spp. mosquitoes that may transmit West Nile virus [and lymphatic filariasis] [and St. Louis encephalitis].
- Kills/Controls] [disease carrying] mosquitoes that may transmit [West Nile], Encephalitis], [Eastern Equine Encephalitis], [EEE]. Culex mosquitoes are the main vectors of West Nile virus. [Encephalitis] alone is not acceptable; the specific type of encephalitis needs to be listed. [Eastern equine encephalitis] [EEE] is not acceptable. *Culiseta melanura* is the main vector of EEE. Thus, for specific claims of diseases, the specific vector needs to be tested.
- Kills] [Controls] adult mosquitoes
- Reduces the adult mosquito population
- Reduces mosquito nuisance
- Larvae [in the trap container] will not develop into adult mosquitoes
- Mosquitoes auto-disseminate larvicide to their breeding sites
- [Kills] [Controls] mosquito larvae in surrounding breeding places
- Prevents mosquitoes from [breeding] [multiplying] [reproducing]
- Keeps mosquito populations at lower levels compared to conventional vector control measures
- Provides [continuous] [longer term[long-lasting] [sustained] mosquito control
- Kills the female mosquito and her offspring
- Claims that reference killing *Culex* larvae or adults
- Auto-dissemination claims by *Culex* or *Aedes* mosquitoes.

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product: n/a

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

~~Outer Bag~~Packaging/Outer Box Labeling –

PYRIPROXYFEN	**GROUP**	**7C**	**INSECTICIDE**
***Beauveria bassiana* Strain GHA**	**GROUP**	**UN**	**INSECTICIDE**

In2Mix®

For Use In The In2Care® Trap

For use to control *Aedes* and *Culex* species of Mosquitoes that may transmit Zika, Chikungunya, ~~and~~ Dengue Fever, encephalitis, or West Nile virus

THIS PRODUCT IS NOT FOR SALE TO OR USE BY HOMEOWNERS

ROOM FOR MARKETING STATEMENTS AND ARTWORK

READ ALL LABEL DIRECTIONS COMPLETELY BEFORE USE

Active Ingredients:	**% w/w**
Pyriproxyfen (CAS No. 95737-68-1).....	74.03%
Beauveria bassiana strain GHA* (CAS No. 63428-82-0).....	10.00%
Other Ingredients:.....	15.97%
Total	100.00%

* Contains not less than 4.5 X 10^9 viable spores/gm.

KEEP OUT OF REACH OF CHILDREN

CAUTION

SEE [SIDE] [BACK] [PANEL] [INSIDE] [LABEL BOOKLET] FOR [FIRST AID], [ADDITIONAL] PRECAUTIONARY STATEMENTS [AND] [COMPLETE] DIRECTIONS FOR USE [INCLUDING STORAGE AND DISPOSAL INSTRUCTIONS

Manufactured [by][for]:
In2Care BV
Marijkeweg 22, 6709 PG,
Wageningen, The Netherlands

EPA Reg. No.: 91720-1
EPA Est. No.: XXXXX-XX-XXX

Net Weight: [~~12.5~~ xx g (~~0.44~~ xx [oz.][ounce])
~~25~~ xx packages x 0.5 g each (~~0.018~~ xx [oz.][ounce])]

~~[25 g (0.88 [oz.][ounce]~~
~~50 packages x 0.5 g each (0.018 [oz.][ounce])]~~

~~[50 g (1.76 [oz.][ounces])~~
~~100 packages x 0.5g each (0.018 [oz.][ounce])]~~

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

PRECAUTIONARY STATEMENTS

HAZARD TO HUMAN AND DOMESTIC ANIMALS

~~Harmful if inhaled, swallowed, or absorbed through skin.~~ Causes moderate eye irritation. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. ~~Repeated exposure to high concentrations of microbial proteins can cause allergic sensitization. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.~~ Remove and wash contaminated clothing before reuse. Obtain medical attention if irritation persists. ~~Avoid contamination of food or feedstuffs.~~

FIRST AID	
~~**If Inhaled**~~	~~Move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. Call a poison control center or doctor for further treatment advice.~~
~~**If Swallowed**~~	~~Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.~~
~~**If on Skin**~~	~~Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.~~
If in Eyes	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. For non-emergency general information on this pesticide product (including health concerns or pesticide incidents), call the poison control center at 1-800-222-1222 ~~after 12:00 P.M. PST on weekdays and during the weekend.~~

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage or disposal.

PESTICIDE STORAGE: Keep this product in its tightly closed original container when not in use. Store in a cool, dry, well-ventilated area that is inaccessible to children and animals. For optimal long-term storage, do not store above 73° F (23° C). Store this product in a place away from strong bases, strong acids, sources of ignition and direct sunlight.

During transport and field use, keep **In2Mix®** packages below 110° F (43° C) at all times by avoiding sunlight and heat, and using isolation packaging.

PESTICIDE DISPOSAL: Dispose of used gauze in a sanitary landfill, or by other procedures approved by state and local authorities. Dispose of used water with attractants by pouring out of **In2Care®** trap onto the ground, and not near a water source. Prevent entry of used water into sewers, gutters, or drains, or any area where drainage to storm sewers, water bodies, or aquatic habitat can occur. Notify authorities if liquid enters sewers or public waters.

CONTAINER HANDLING: Completely empty **In2Mix®** package into the **In2Care®** trap by shaking and tapping sides and bottom to loosen clinging particles. When completely empty, dispose of empty package in trash or by other procedures approved by state and local authorities.

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

Label Booklet –

PYRIPROXYFEN	**GROUP**	**7C**	**INSECTICIDE**
***Beauveria bassiana* Strain GHA**	**GROUP**	**UN**	**INSECTICIDE**

In2Mix®

For Use In The In2Care® Trap

For use to control *Aedes* ~~and *Culex*~~ species of Mosquitoes that may transmit Zika, Chikungunya, ~~and~~ Dengue Fever, encephalitis, or ~~West Nile virus~~

ROOM FOR MARKETING STATEMENTS AND ARTWORK

THIS PRODUCT IS NOT FOR SALE TO OR USE BY HOMEOWNERS

SHAKE In2Mix® PACKAGE BEFORE USE

READ ALL LABEL DIRECTIONS COMPLETELY BEFORE USE

Active Ingredients:	**% w/w**
Pyriproxyfen (CAS No. 95737-68-1).....	74.03%
Beauveria strain GHA* (CAS No. 63428-82-0).....	10.00%
Other Ingredients:.....	15.97%
Total	100.00%

* Contains not less than 4.5 X 10^9 viable spores/gm.

KEEP OUT OF REACH OF CHILDREN

CAUTION

SEE INSIDE LABEL BOOKLET FOR [FIRST AID], [ADDITIONAL] PRECAUTIONARY STATEMENTS AND COMPLETE DIRECTIONS FOR USE INCLUDING STORAGE AND DISPOSAL INSTRUCTIONS.

Manufactured [by][for]:
In2Care BV
Marijkeweg 22, 6709 PG,
Wageningen, The Netherlands

EPA Reg. No.: 91720-1
EPA Est. No.: XXXXX-XX-XXX

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

PRECAUTIONARY STATEMENTS

HAZARD TO HUMAN AND DOMESTIC ANIMALS

~~Harmful if inhaled, swallowed, or absorbed through skin.~~ Causes moderate eye irritation. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. ~~Repeated exposure to high concentrations of microbial proteins can cause allergic sensitization. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.~~ Remove and wash contaminated clothing before reuse. Obtain medical attention if irritation persists. ~~Avoid contamination of food or feedstuffs.~~

FIRST AID	
~~**If Inhaled**~~	~~Move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. Call a poison control center or doctor for further treatment advice.~~
~~**If Swallowed**~~	~~Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.~~
~~**If on Skin**~~	~~Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.~~
If in Eyes	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
HOT LINE NUMBER Have the product container or label with you when calling a poison control center or doctor or going for treatment. For non-emergency general information on this pesticide product (including health concerns or pesticide incidents), call the poison control center at 1-800-222-1222 ~~after 12:00 P.M. PST on weekdays and during the weekend~~.	

PERSONAL PROTECTIVE EQUIPMENT (PPE)

All applicators and handlers must wear:

- Short~~Long~~-sleeved shirt and short~~long~~ pants;
- Waterproof gloves; and
- Shoes plus socks
- ~~In addition, all applicators and handlers must wear a NIOSH-approved particulate respirator with any N, R, or P filter (NIOSH approval number prefix TC-84A); or a NIOSH-approved powered air purifying respirator with an HE filter (NIOSH approval number prefix TC-21C).~~

Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry.

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USER SAFETY RECOMMENDATIONS

Users should:

• Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.

• Remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

• Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

This product is toxic to fish and aquatic invertebrates. Do not apply directly to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment wash-waters. Application of this product is prohibited directly into sewers or drains, or to any area like a gutter where drainage to storm sewers, water bodies, or aquatic habitat can occur. Do not allow the product to enter any drain during or after application.

This product is highly toxic and may be pathogenic to bees ex posed to direct treatment on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds while bees are actively visiting the treatment area.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

READ ALL LABEL DIRECTIONS COMPLETELY BEFORE USE.

SHAKE In2Mix® PACKAGE BEFORE USE.

FOR OUTDOOR USE ONLY.

DO NOT allow people or pets to contact the pesticide.

HOW IT WORKS

In2Mix® powder contains a growth regulator and slow acting adulticide.

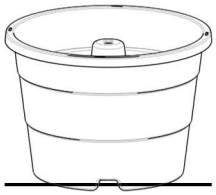
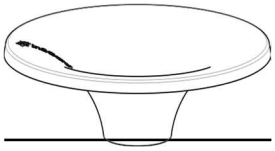
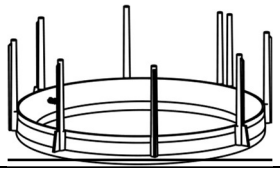
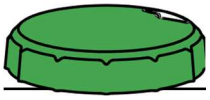
The growth regulator kills the *Aedes* ~~and *Culex*~~ spp. larvae that emerge from eggs laid inside the trap prior to transforming into adults. This means that it is normal to see small living larvae in the trap that will eventually die.

After laying eggs, the adult *Aedes* ~~and *Culex*~~ spp. mosquito is contaminated with the **In2Mix®** powder. When they fly out of the trap to lay more eggs elsewhere, they disseminate the growth regulator and kill larvae in breeding sites around the trap.

The adulticide contained in the **In2Mix®** powder slowly kills adult *Aedes* ~~and *Culex*~~ spp. mosquitoes. Contaminated mosquitoes will die within a few days following exposure to **In2Mix®** powder. Therefore, dead adult mosquitoes may not be found in the trap.

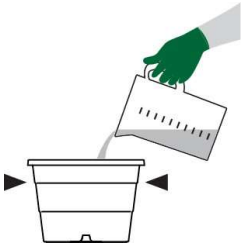
Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

HOW TO ASSEMBLE

				
In2Mix® package	**Base**	**Lid**	**Floater**	**Time indicator cap**

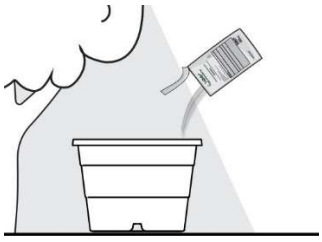
STEP 1:

1. Fill the base of the trap with 5 quarts (4.7 liters) of clean tap water.



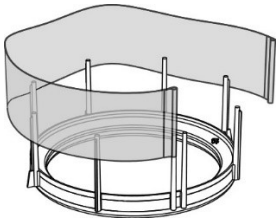
2. **SHAKE THE In2Mix® PACKAGE THOROUGHLY**. Open by tearing at the notches and gently take out the powder-coated gauze strip.

3. Empty the remaining contents (powder and odor tablets) of the **In2Mix®**package into the water in the base of the trap. Do not allow the gauze to get wet.

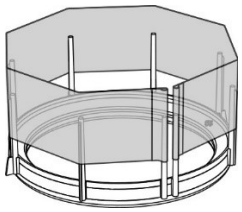


STEP 2:

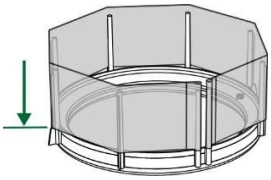
1. To attach the **In2Mix®** gauze strip to the floater, slide the loop at the end of the gauze over the pin as shown. Try not to touch the gauze extensively to avoid removal of the active powders.



2. Wrap the gauze around the floater and slide the other gauze loop on the last pin as shown. Work your way around moving the gauze down at each pin.

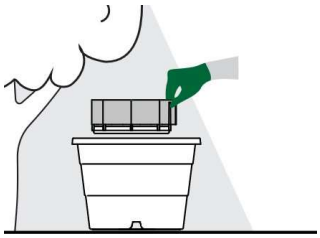


3. Push the gauze down the pins until it will go no further (where the bottom of the pin hits the circular rib). The rib will prevent the gauze from sliding down too far.

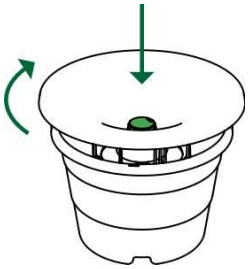


STEP 3:

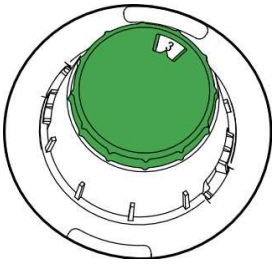
1. Place the assembled floater inside the base of the trap by gently placing it over the central tube flat onto the water. Do not allow the gauze to get wet as water will degrade the powder.



2. Place the lid on the central tube, push it down and turn it clockwise.

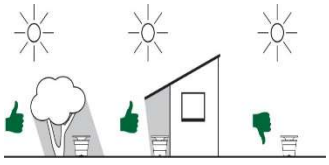


3. Turn the time indicator to the number of the current month as a service reminder. Use one **In2Mix®** package per trap every 4 ~~to 6~~ weeks when adult mosquitoes are active.



WHERE TO PLACE

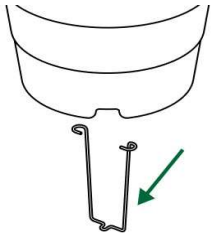
1. Place the water-filled **In2Care®** trap outside on the ground in a level, shaded location near human habitation. Avoid locations with direct sunlight; continuous shade is needed.



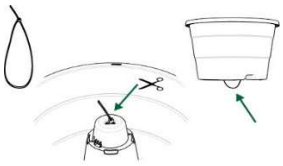
For best results, remove and/or empty artificial water containers (e.g., flowerpots, plastic cups, car tires, etc.) and natural breeding sites (e.g., puddles, tree holes, etc.). Larger water bodies that cannot be removed or emptied should be (frequently) treated with appropriate mosquito larvicides.

2. For optimal coverage, place at least 1 **In2Care®** trap every 4,300 sq. feet (400 sq. meters), or at least 10 traps per acre in areas where Aedes mosquitoes breeding can be expected. Do not exceed 15 traps per acre.

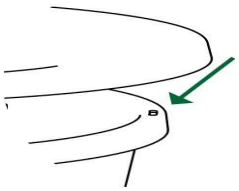
3. When necessary, stability can be improved by securing the trap to the ground with the following:



   a. Wire bracket, available separately from the distributor, which snaps onto the base. The wire bracket can be screwed onto a surface or fixed with a ground pin.



   b. Zip tie (not included). Zip Tie spec: width: 4.8mm length: 600mm. The loop can be tied to a pin or hook.



   c. The base may also be attached to a pole, shrub or tree by using zip ties or a small rope tied through the holes in the rim of the base.

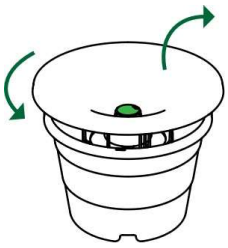
NOTE: *Aedes* ~~and *Culex*~~ spp. mosquitoes can have very specific breeding preferences within certain locations. Check for the presence of live and dead mosquito larvae inside the traps every 4 ~~to 6~~ weeks. When a trap continuously has zero or much fewer larvae when compared to other nearby traps, the unattractive trap should be relocated to another nearby shaded location.

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

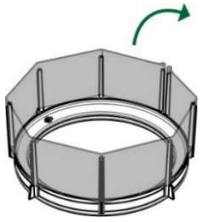
MAINTAINING THE TRAP

1. Re-visit each **In2Care®** trap every 4 ~~to 6~~ weeks. Remove the lid by turning it counterclockwise until it stops and lift up.

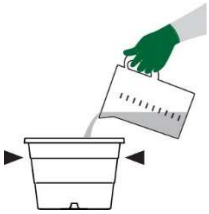
   NOTE: In hot and dry climates the water level must be checked more frequently. Add water as necessary to maintain the correct amount (5 quarts; 4.7 liters) in the base of the trap.



2. Take out the floater and dispose of the used gauze and water as indicated in the **STORAGE AND DISPOSAL** section of this label.



3. Remove leaves or other debris that may have fallen into the base of the trap. Refill the trap with 5 quarts (4.7 liters) of clean tap water.



4. Take a new **In2Mix®** package and repeat **Steps 1 & 2** in **HOW TO ASSEMBLE.**

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage or disposal.

PESTICIDE STORAGE: Keep this product in its tightly closed original container when not in use. Store in a cool, dry, well-ventilated area that is inaccessible to children and animals. For optimal long-term storage, do not store above 73° F (23° C). Store this product in a place away from strong bases, strong acids, sources of ignition and direct sunlight.

During transport and field use, keep **In2Mix®** packages below 110° F (43° C) at all times by avoiding sunlight and heat, and using isolation packaging.

PESTICIDE DISPOSAL: Dispose of used gauze in a sanitary landfill, or by other procedures approved by state and local authorities. Dispose of used water with attractants by pouring out of **In2Care®** trap onto the ground, and not near a water source. Prevent entry of used water into sewers, gutters, or drains, or any area where drainage to storm sewers, water bodies, or aquatic habitat can occur. Notify authorities if liquid enters sewers or public waters.

CONTAINER HANDLING: Completely empty **In2Mix®** package into the **In2Care®** trap by shaking and tapping sides and bottom to loosen clinging particles. When completely empty, dispose of empty package in trash or by other procedures approved by state and local authorities.

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

NOTICE: Buyer and user assume all risks and liability of use, storage and/or handling of this product not in accordance with the terms of this label.

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Individual refill package labeling –

PYRIPROXYFEN	**GROUP**	**7C**	**INSECTICIDE**
***Beauveria bassiana* Strain GHA**	**GROUP**	**UN**	**INSECTICIDE**

In2Mix®

For Use In The In2Care® Trap

ROOM FOR MARKETING STATEMENTS AND ARTWORK

SHAKE WELL BEFORE USE

Active Ingredients:	**% w/w**
Pyriproxyfen (CAS No. 95737-68-1)……	74.03%
Beauveria bassiana strain GHA* (CAS No. 63428-82-0)……	10.00%
Other Ingredients:……	15.97%
Total	100.00%

* Contains not less than 4.5 X 10^9 viable spores/gm.

KEEP OUT OF REACH OF CHILDREN

CAUTION

SEE LABEL BOOKLET FOR ADDITIONAL PRECAUTIONARY STATEMENTS AND COMPLETE DIRECTIONS FOR USE

Manufactured [by][for]:
In2Care BV
Marijkeweg 22, 6709 PG,
Wageningen,
The Netherlands

EPA Reg. No.: 91720-1
EPA Est. No.: XXXXX-XX-XXX

Net Weight: 0.5g (0.018 [oz.][ounce])

Bracketed "[]" text is optional text; bold italicized text is information for the reader and is not part of the label

PRECAUTIONARY STATEMENTS

HAZARD TO HUMAN AND DOMESTIC ANIMALS

~~Harmful if inhaled, swallowed, or absorbed through skin.~~ Causes moderate eye irritation. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. ~~Repeated exposure to high concentrations of microbial proteins can cause allergic sensitization. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.~~ Remove and wash contaminated clothing before reuse. Obtain medical attention if irritation persists. ~~Avoid contamination of food or feedstuffs.~~

FIRST AID	
~~**If Inhaled**~~	~~Move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. Call a poison control center or doctor for further treatment advice.~~
~~**If Swallowed**~~	~~Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.~~
~~**If on Skin**~~	~~Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.~~
If in Eyes	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. For non-emergency general information on this pesticide product (including health concerns or pesticide incidents), call the poison control center at 1-800-222-1222~~ after 12:00 P.M. PST on weekdays and during the weekend~~.

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage or disposal.

PESTICIDE STORAGE: Keep this product in its tightly closed original container when not in use. Store in a cool, dry, well-ventilated area that is inaccessible to children and animals. For optimal long-term storage, do not store above 73° F (23° C). Store this product in a place away from strong bases, strong acids, sources of ignition and direct sunlight.

During transport and field use, keep **In2Mix®** packages below 110° F (43° C) at all times by avoiding sunlight and heat, and using isolation packaging.

PESTICIDE DISPOSAL: Dispose of used gauze in a sanitary landfill, or by other procedures approved by state and local authorities. Dispose of used water with attractants by pouring out of **In2Care®** trap onto the ground, and not near a water source. Prevent entry of used water into sewers, gutters, or drains, or any area where drainage to storm sewers, water bodies, or aquatic habitat can occur. Notify authorities if liquid enters sewers or public waters.

CONTAINER HANDLING: Completely empty **In2Mix®** package into the **In2Care®** trap by shaking and tapping sides and bottom to loosen clinging particles. When completely empty, dispose of empty package in trash or by other procedures approved by state and local authorities.

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Optional Marketing Claims to be used on any of the included sublabels

Note to PM: When qualified claims are used on the market label, the qualifying statement will appear in close proximity to the claim when it does not impact any mandatory language.

Note to PM: Any combination of approved claims may be inserted.

INSECTICIDAL/EFFICACY CLAIMS

1. ~~Controls container-breeding *Culex* spp. mosquitoes that may transmit West Nile virus [and lymphatic filariasis] [and St. Louis encephalitis]~~
2. Kills/Controls] [disease carrying] mosquitoes that may transmit [Zika virus] ~~[West Nile], [Encephalitis], [Eastern Equine Encephalitis], [EEE~~]
3. ~~Attracts mosquitoes during their breeding cycle~~
4. [Kills] [Controls] adult mosquitoes
5. ~~Reduces the adult mosquito population~~
6. ~~Reduces mosquito nuisance~~
7. ~~Larvae [in the trap container] will not develop into adult mosquitoes~~
8. ~~Mosquitoes auto-disseminate larvicide to their breeding sites~~
9. ~~[Kills] [Controls] mosquito larvae in surrounding breeding places~~
10. ~~Prevents mosquitoes from [breeding] [multiplying] [reproducing]~~
11. ~~Keeps mosquito populations at lower levels compared to conventional vector control measures~~
12. ~~Provides [continuous] [longer term] [long-lasting] [sustained] mosquito control~~
13. Effective up to ~~6~~ weeks before replacement of active ingredients is needed
14. ~~Kills the female mosquito and her offspring~~
15. Refill sachets can be stored at least one year [at room temperature] [at 77 ± 3 ° Fahrenheit] [at 25 ± 2 ° Celsius]

PACKAGE/EASE OF USE/LOCATION CLAIMS

1. [Effective] For outdoor use
2. [Ideal] [Great] [Use] for mosquito control in your yard
3. Ideal for use [in yards] [in gardens] [in parks] [near ponds][on lawns] [on outdoor patios] [on outdoor decks]
4. Does not release unpleasant odors
5. No noises/ sounds [coming from the trap]
6. Easy to [set up] [assemble] [use] [install]
7. Quick/Easy to [maintain] [service]
8. Securable lid
9. Light-weight plastic container
10. Convenient floater/sachet replacement timer
11. Container made of recycled plastic

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12. No batteries or electricity required
13. Two active ingredients in one product
14. Dual action
15. Can be used [in combination] with other mosquito control tools
16. Durable plastic for long employment of the trap container
17. Rugged and durable design
18. Recycled plastic used for production of the plastic trap container
19. Patented technology
20. Innovative [mosquito] control tool
21. Uses the mosquitoes natural [instinct] [behavior] to kill them
22. [Scientific] Proven efficacy against mosquitoes
23. Residual control that lasts up to ~~6~~ weeks
24. Reduces environmental impacts by minimizing the use of active ingredients
25. Uses fewer chemicals than fogging with adulticides
26. Reduces [impacts on] [exposure to] other insects such as butterflies and bees [by limiting the use of active ingredients inside the trap container]
27. Environmentally friendly solution to kill mosquitoes

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Packaging/Outer Box Labeling –

PYRIPROXYFEN	**GROUP**	**7C**	**INSECTICIDE**
***Beauveria bassiana* Strain GHA**	**GROUP**	**UN**	**INSECTICIDE**

In2Mix®

For Use In The In2Care® Trap

For use to control *Aedes* ~~and *Culex*~~ species of Mosquitoes that may transmit Zika, Chikungunya, Dengue Fever, ~~encephalitis, or West Nile virus~~

THIS PRODUCT IS NOT FOR SALE TO OR USE BY HOMEOWNERS

ROOM FOR MARKETING STATEMENTS AND ARTWORK

READ ALL LABEL DIRECTIONS COMPLETELY BEFORE USE

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SEE [SIDE] [BACK] [PANEL] [INSIDE] [LABEL BOOKLET] FOR [FIRST AID], [ADDITIONAL] PRECAUTIONARY STATEMENTS [AND] [COMPLETE] DIRECTIONS FOR USE [INCLUDING STORAGE AND DISPOSAL INSTRUCTIONS

Manufactured [by][for]:
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Wageningen, The Netherlands

EPA Reg. No.: 91720-1
EPA Est. No.: XXXXX-XX-XXX

Net Weight: [xx g (xx [oz.][ounce])
xx packages x 0.5 g each (xx [oz.][ounce])]

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